Perinatal bacterial infection: screening of vertical transmitted infections

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Hospital Dona Estefânia, Lisbon. Founded in 1860

Summary

- The rational for screening
- Why some countries have a non-screening policy
- Risk factors: a very useful complement of screening
- Conclusions

The burden of the problem

- Incidence of early-onset neonatal infection may vary between 0.98 to 1.2 or 1.3/1000 live births *(Stoll B, Kuhn P, Lin C-Y)*
- Lethality vary between 1.8% and 16% ((Kuhn, Stoll).
- Mortality depends on gestational age and isolates: 30% in newborns 25-28 weeks; 33% in E. Coli vs 9% for GBS *(Barbara Stoll, 2011)*

Early-onset bacterial neonatal infection

Caused by bacteria colonising the birth canal

- Gram positive isolates:
  Group B *Streptococcus* but also *Streptococcus pneumoniae*, *Enterococcus* , *Listeria*
- Gram negative isolates:
  Enterobacteriacea - *E. coli* but also *Proteus* spp, *Klebsiella* spp, *Haemophylus*

- Vergnano S et al. Arch *Dis Child Fetal Neonatal* Ed 2011 UK
- Kuhn P et al . Paediatric and Perinatal Epidemiol 2010 France
- Stoll BJ et al. *Pediatrics* 2011 – USA
- Lin CY et al. *Pediatr Neonatol* 2011 – Taiwan.
- Al-Taiar A et al. International J Infectious Dis 2011 Kuwait

Early-onset bacterial neonatal infection

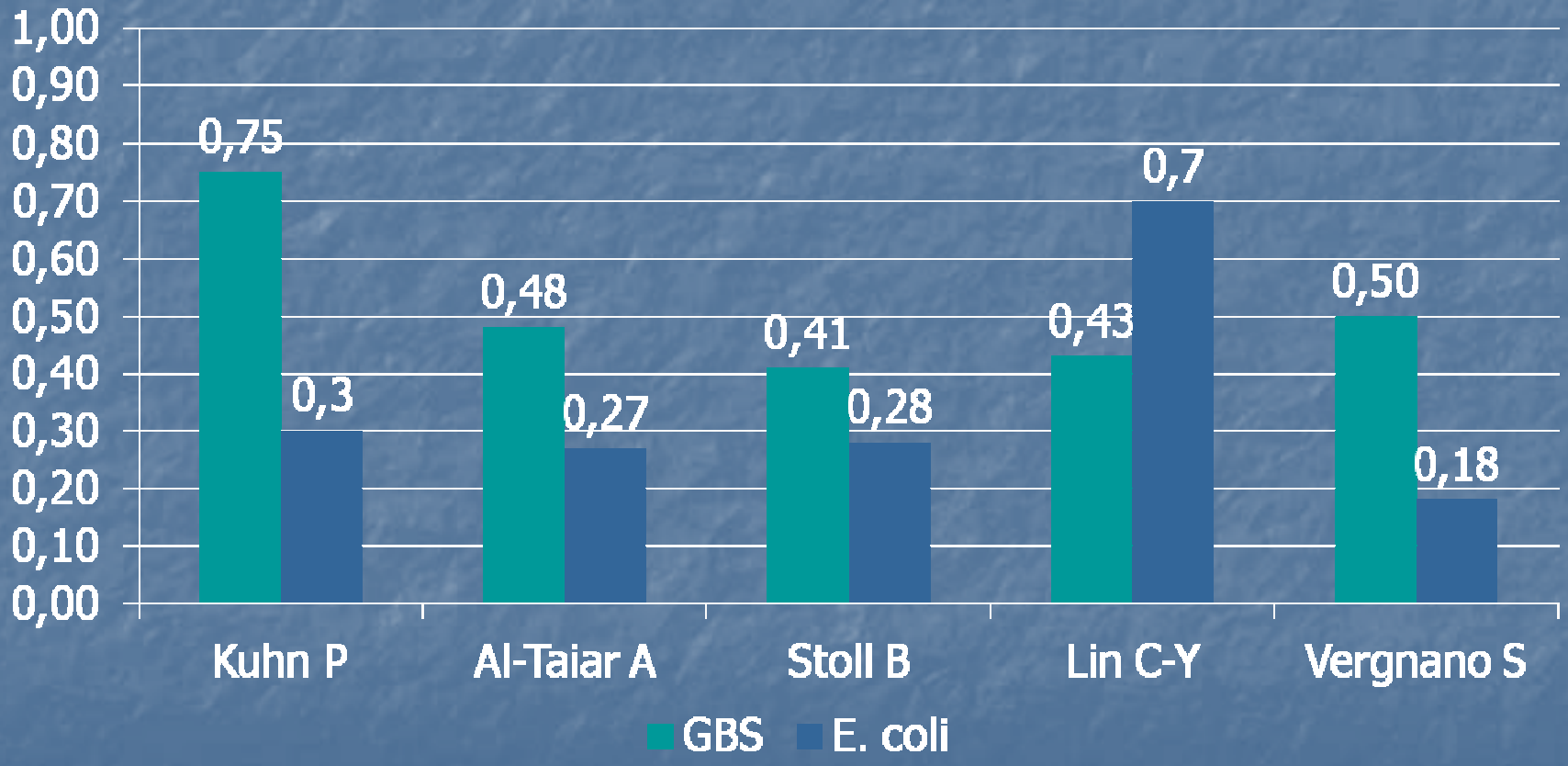
- In the past Enterobacteriacea, mostly *E. coli*, were accepted as the most common cause of early-onset (EOS) neonatal bacterial infection
- In the 1970s GBS infections emerged as the leading cause of EOS and meningitis (and E. Coli was forgotten?)

Portuguese National Prevalence Study

One day surveillance - 2010

	Ner of patients	Bacteria
Newborns in the postnatal ward	567	*Enterococcus faecalis* – 1
Newborns in NICU	287	*E. coli* – 6 GBS – 2 *Streptococcus pneumoniae* – 1 *Proteus mirabilis* – 1
Patients >28 days Infections in patients admitted from home	20270	*E.coli* - 320 GBS – 22 *Listeria* -2

Incidence of early-onset infection caused by GBS and *E. coli* /1000 births



Sepsis caused by possible mother-acquired bacteria in newborn infants admited to NICUs

Portuguese surveillance system data

	2008	2009	2010	Total
Patients	5369	5058	4911	15338
GBS	34 6.3/1000	27 5.3/1000	20 4.1/1000	81 (5/1000)
E. coli	37 6.9/1000	39 7.7/1000	24 4.9/1000	100 (7/1000)
Listeria	6	0	4	10 (0.7/1000)

GBD early-onset infection

- Since 1992 AAP guidelines advise screening and prevention of GBS vertical transmission aiming to decrease early-onset infection.
- These guidelines were adopted by several countries and denied by others
- No studies on screening and prophylaxis for *E. coli* are known

The Portuguese studies
PPSU

- Group B streptococcal disease in Portuguese infants younger than 90 days

Enrolling only septic newborn infants with positive cultures in sterile fluids * (2001-2004)

- Group B streptococcal disease – the hidden cases

Enrolling newborn infants with proven and possible GBS infection (2006-2007)

* *Neto MT Arch. Dis. Child. Fetal Neonatal Ed. 2008;93;90-93*

** *Neto MT Non-published data*

Compared data

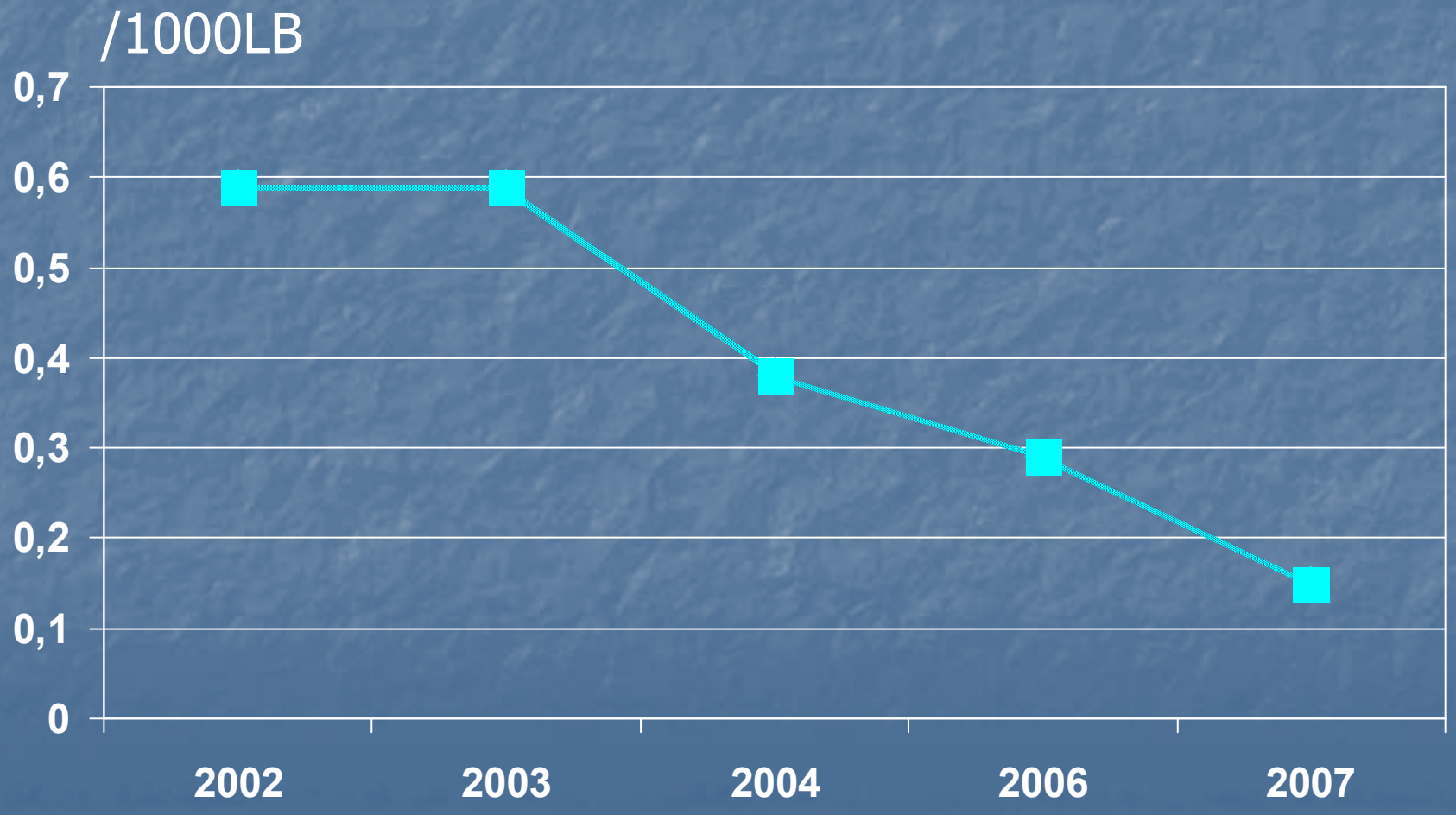
	First study	Second study
Incidence of early-onset proven infection	0.44/1000LB	0.22/1000LB
Early-onset infection	83%	66%

Incidence

Per complete years, in the two studies

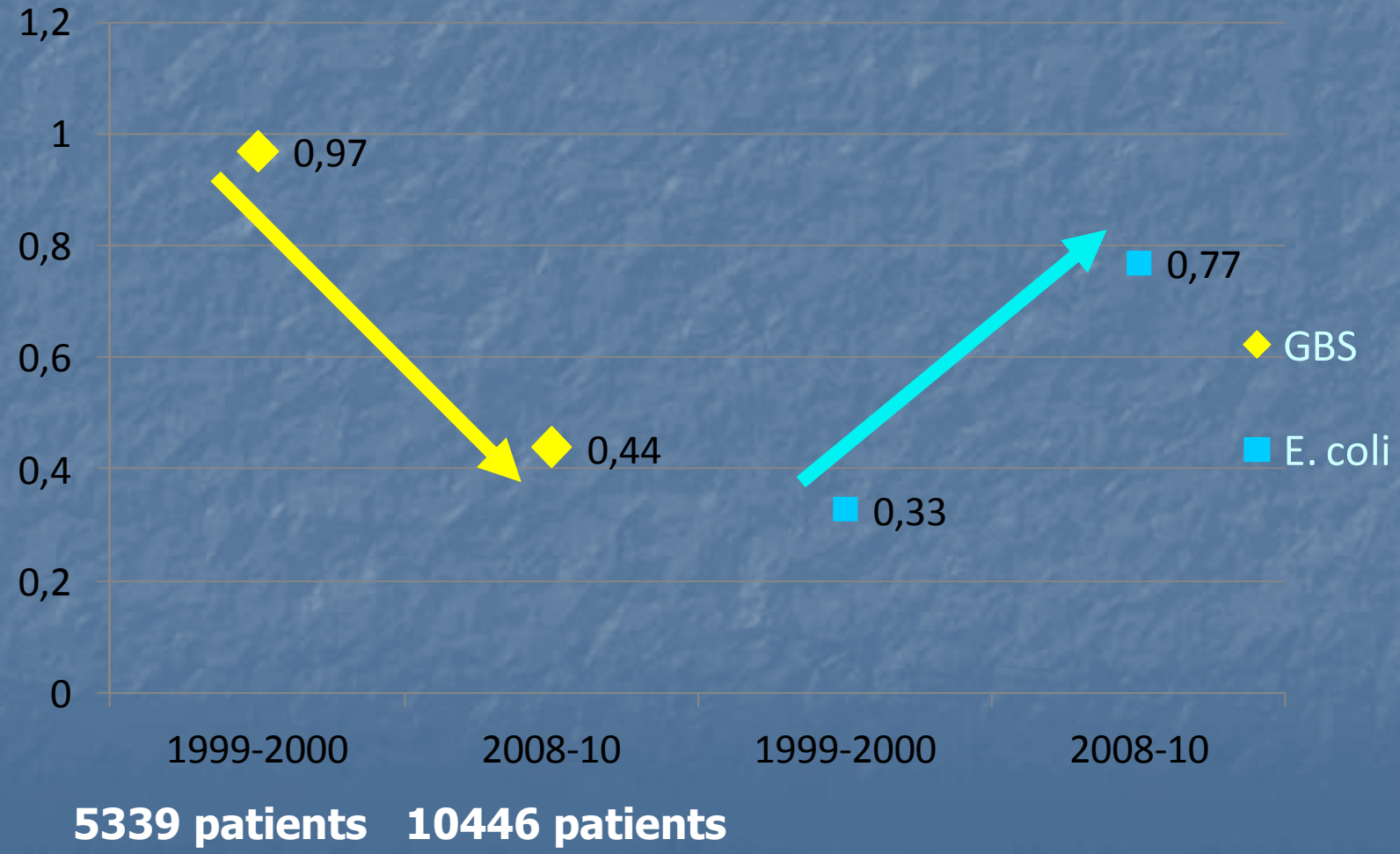
Proven infection only

Casualty or effects of screening and prophylaxis?



GBS and *E. coli* positive blood cultures in Portuguese NICU in two different periods

(in % of admitted newborn infants)



Conclusions of two important studies on universal GBS screening and prophylaxis

- Rates of GBS infection declined but reflect a continued burden of disease. GBS continues the most frequent pathogen in term infants and *E. Coli* the most frequent in preterm infants
- *Stoll BJ et al. Pediatrics 2011 – USA.*
- GBS screening and prophylaxis is effective in decreasing the incidence of GBS EOS; however an increase in EOS caused by E. Coli was noted.

Lin CY et al. Pediatr Neonatol 2011 – Taiwan.

Is there a reason to screen? Yes!

However, even today, against all grades of evidence, some countries do not have national guidelines

Why?

Bias related to carriers

- Colonization is intermittent
- Prevalence of carriers varies with geographic areas making obsolete national guidelines. In Portugal it is about 30% in the North and 12% in the South*

**Neto MT, 2009*

Bias related to screening

- Screening should be done by 35/36 gestational week – preterm delivery is excluded
- Vaginal and rectal swabs should be done – many women only have a vaginal swab – false negative
- Specification on request should be done – false negative
- Transport and culture should be appropriate - false negative
- Once a national guideline is implemented it should be accomplished all over the country with uniform high quality

Bias related to prophylaxis

- Time before birth is needed
- Penicillin is the antibiotic of choice.
- GBS resistance to some of the alternatives have been reported – 10% to erythromycin in a Portuguese study*
- Early-onset infection may occur in newborn infants whose mothers were given correct prophylaxis

** Exposto F. Non-published data*

Newborn infants with early-onset GBS infection
Screening and prophylaxis

	Neto MT	**Stoll B**
Screened mothers	61%	58%
Negative screening	28%	81% in term and 26% in PT
Intrapartum Antibiotics	28%	53% all EOS

Newborns with early-onset infection and mother's prophylaxis

Proven and possible infection - n=57

Positive	Complete prophylaxis	1 dose of antibiotics	None
19	7* (37%)	9	3

* One infant with positive blood culture

Bias related to those conditions supposed to protect that do not

Proven and possible GBS early-onset infection	Caesarean section
57	24 (42%)*

* 14 (58%) with positive blood culture

Screening and prophylaxis
Summarizing confounding factors
Reasons for non-screening policies

- Newborn infants with early-onset infection born to supposed negative mothers
- Newborn infants with early-onset infection born to mothers with complete prophylaxis
- Newborn infants with early-onset infection born by caesarean section

If screening has so many problems should prophylaxis be based on risk factors?

Newborn infants with early-onset proven infection
Known risk factors

Non-screened mothers with risk factors	57 (29%)
Term newborn infants with early-onset infection and risk factors	35/160 (22%) *

Conclusion: Prophylaxis based on risk factors would have missed 71% of all newborn infants and 78% of term newborns with early-onset infection

P.J.Steer and J Plumb found that only 60% of newborn infants with EOGBS disease had risk factors apparent at labour

(Semin Fetal Neonatal Med 2011;16: 254-8)

Common-sense proposals

- Screening should be correctly performed - rectal and introit swabs, selective medium
- Women should know the meaning of carrier state in order to go to the maternity on time to start prophylaxis
- Antibiotics should be started as soon as possible instead of awaiting for a schedule

Common-sense proposals

- GBS carrier state should not be considered the only main risk for early-onset neonatal infection.
- Other risk factors have to be considered even if there is a negative GBS screening – maternal fever, prolonged rupture of membranes, laboratory signs of mother´s infection deserve attention and prophylaxis or treatment
- In any case we know some cases will be missed

Final conclusions

- Screening and intrapartum antibiotics, result in a significant decrease of EOGBS disease. However GBS infection still exists. Better screening and prophylaxis and avoidance of missed opportunities to prevent neonatal infection are desirable
- *E. coli* is the second most common bacteria causing EOS and its importance should not be disregarded mainly in preterm infants
- Monitoring of pathogens causing EOS continues an important issue
- Adding screening to risk factors seems to be a valuable policy to improve prevention of EOS